e- ISSN 0976-0342
Print ISSN 2229-7456

International Journal of Pharmacy & Therapeutics

Journal homepage: www.ijptjournal.com

Review article

ALICE IN WONDERLAND SYNDROME: A REVIEW

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ABSTRACT

Alice in Wonderland Syndrome, also known as Todd's syndrome or Lilliputian hallucinations, is a rare disorienting neuropsychological condition that affects perception. The syndrome was originally coined by Dr. John Todd in 1955 and was named after the sensations experienced by the character Alice in Lewis Carroll's novel "Alice's Adventures in Wonderland". AIWS can occur at any age but mostly in children less than 18 years old. The symptoms of AIWS include metamorphopsia, bizarre distortions of their body image, and bizarre perceptual distortions of form, size, movement or color. Additionally, patients can experience auditory hallucinations and changes in their perception of time. This syndrome has many different etiologies such as Epstein-Barr virus infection, migraine, temporal lobe epilepsy, brain tumours and psychostimulant drugs. Auxiliary investigations including blood tests, brain MRI and EEG are strongly advised for the diagnosis of AIWS. The long-term prognosis typically depends on the root cause of the syndrome, and the underlying chronic conditions such as migraine and epilepsy must be evaluated and treated. Alice in Wonderland Syndrome has no proven, effective treatment. Whenever treatment is considered useful and necessary, it needs to be aimed at the suspected underlying condition. Further research is required to establish an effective treatment regimen.

Key Words:- Alice in Wonderland Syndrome, Metamorphopsia, Epstein - Barr virus, Temporal lobe epilepsy.

Access this article online

Home page: http://ijptjournal.com/

DOI: http://dx.doi.org/10.21276/ijpt.2019.10.3.1

Quick Response code

Received:27.02.19 **Revised**:05.03.19 **Accepted**:14.03.19

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INTRODUCTION

Alice in Wonderland Syndrome (AIWS) is a rare neuropsychological condition, defined by the presence of paroxysmal distortion of the body schema, depersonalization, derealisation, visual hallucination and distorted sense of time experiences (Azimova JE *et al*., 2016). The syndrome was originally coined by Dr. John Todd in 1955 and was named after the sensations experienced by the character Alice in Lewis Carroll's novel "Alice's Adventures in Wonderland" (Blom JD, 2016). AIWS can occur at any age but mostly in children less than 18 years old (Blom JD, 2016). The syndrome have many symptoms that shows both diagnostic and therapeutic consequences, differ substantially from those in schizophrenic disorders and other hallucinatory syndromes (Blom JD, 2016).

Patients with AIWS can experience both clinical as well as non-clinical symptoms (Blom JD, 2016; Palacios-Sanchez L *et al*., 2018). AIWS is poorly known and misdiagnosed syndrome. No accepted diagnostic criteria have been made for this neuropsychological condition (Mastria G *et al*., 2016).

EPIDEMIOLOGY

No epidemiological datas are available and it is considered as a rare syndrome. Clinical studies among patients with migraine showed that the prevalence rate of this group is around 15% (Blom JD, 2016).

ETIOLOGY

The etiological factors are classified into various groups. The most common cause is migraine (Blom JD, 2016; Mastria G *et al*., 2016). AIWS can also be developed in non- migraineurs, especially in patients who have infectious disease associated with fever (Azimova JE *et al*., 2016). Most common causes reported (Blom JD, 2016; Mastria G *et al*., 2016).

AIWS Etiologies:

- Headache
  - Migraine
  - Abdominal Migraine
  - Cluster headache
  - Tension type headache
  - HANDL: Syndrome of transient headache with neurologic deficits and CSF lymphocytosis.
- Epilepsy
  - Temporal lobe epilepsy
  - Frontal lobe epilepsy
- Infectious disease
  - Coxsackie B_1 virus encephalitis
  - Cytomegalovirus
  - Epstein Barr virus encephalitis
  - Influenza A virus encephalitis
  - Lyme neuroborreliosis
  - Scarlet fever
  - Typhoid encephalopathy
  - Varicella Zoster encephalitis
  - Mycoplasma
  - Parainfective vasculitis
- Cerebrovascular Disease
  - Intraparenchymal haemorrhagic stroke
  - Ischemic stroke
  - Cavernous angioma
  - Cerebral haemorrhage
  - Cerebral infarction
  - Pituitary infarction
  - Brain tumour
  - Wallenberg syndrome
- Other brain disease includes
  - Acute disseminated encephalomyelitis
  - Glioblastoma
- Psychiatric disorders
  - Depressive disorders
  - Derealization
  - Misidentification syndrome
  - Cotard's Syndrome
  - Capgras Syndrome
  - Schizophrenia
  - Schizoaffective disorder
- Medications
  - Dextromethorphan
  - Montelukast
  - Topiramate
  - LSD
  - Toluene based solvent
  - Oseltamivir
  - Cocaine
  - Cannabis
  - Risperidone
  - Amphetamines
  - Amanita muscaria
- Miscellaneous
  - Hypnagogic state
  - Hypnopomic state
  - Hypnotherapy
  - Hyperpyrexia
  - Sensory deprivation

CLINICAL MANIFESTATIONS

AIWS usually develops during the childhood; precursor for the syndrome is migraine. Syndrome does not have any relationship with the sex; except for migraine associated cases, where females are more prevalent (Palacios-Sanchez L *et al*., 2018). The syndromes are characterised as follows: Micropsia (objects appear smaller than normal), Macropsia (objects appear larger than normal), Achromatopsia (strongly diminished ability to perceive color), Erythropsia (red vision), Polyopia (multiple identical copies of a single image), Palinopsia (illusory recurrence of visual percepts), optic allesthesia (transposition of visual images from one half of the visual field to the other), inverted vision, loss of stereoscopic vision, alterations in hearing, depersonalization, distorted perception of time, visual hallucinations, autokinesia and somatophycic duality (Azimova JE *et al*., 2016; Lahat E *et a*l., 1991). These symptoms can be occur several times during the day and lasts for less than 24 hours. Sometimes, it develops towards chronicity (Palacios-Sanchez L *et al*., 2018).

Classification of AIWS based on symptoms

TYPE-A: Patients with somesthetic symptoms such as Macrosomatognosia or microsomatognosia, paraschematia.

TYPE-B: Patients with visual illusions such as micropsia, macropsia, telopsia.

TYPE-C: Both Type A and Type B symptoms (Mastria G *et al*., 2016).

Anatomical Correlation with Symptoms of Aiws

Few studies have shown that in some patients with AIWS, damage occurs at the cerebral cortices. The major area for developing AIWS is at TPO-C. TPO-C, is the cross road of temporooccipital, parietooccipital, and temporoparietal junctions. It helps in the integration of visual and somatosensory information to form an inner and external representation of self (Mastria G *et al*., 2016). If a lesion occurs in occipital region, patient may experience visual disturbances, where as if the lesions are observed in parietal and temporal areas, patient may develop both somatosensory and cognitive disorders

along with the visual illusions, finally leads to more complex symptoms (Mastria G *et al*., 2016). When the lesion affects the medial part of occipital lobe and the lingual and fusiform gyri, leads to the development of symptom known as Hemimacropsia (Montalvo MJ, Khan MA, 2014; Park MG *et al*., 2007). AIWS, also have a close association with other neurological or psychiatric disorders.

Symptoms/disorder	Diagnostic tool	Impression
Cotard's Syndrome	PET MRI	Decreased frontoparietal activity. One major left parietal lesions.
Micropsia	SPECT	Hypoperfusion of frontal and frontoparietal areas.
Microsomatognosia, macrosomatognosia, telopsia	SPECT	Hypoperfusion in the frontoparietal operculum.
Macrosomatognosia and microsomatognosia	CT	Focal frontal lobe infarct in the superior right frontal gyrus and the genu of corpus callosum.
Micropsia in child with AIWS	MRI	Hypoactivation in occipital lobe and hyperactivation in right superior parietal cortex (Mastria G *et al*., 2016).

DIAGNOSIS

In clinical practice, AIWS can be diagnosed by a thorough physical examinations (include neurologic, otologic and ophthalmic), taking patients full history and also with the help of the knowledge about various etiological factors associated with the syndrome. Auxillary tests such as blood tests, EEG and brain MRI can be used for diagnosing the cases with suspected etiologies (Blom JD, 2016).

For Examples:

- Epilepsy can be diagnosed by using an Electroencephalogram (EEG) (Palacios-Sanchez L *et al*., 2018).
- Infectious disease – diagnosed by using haematological and serological findings (Lahat E *et a*l., 1991).

Diagnostic criteria are available for migraine related AIWS (Valenca MM et al., 2015):

- One or more episodes of self-experienced body schema illusions or metamorphopsia
- Duration <30 minutes
- Accompanied by headache or a history of migraine
- RMI, CSF and EEG are normal

General steps involved in the diagnosis of AIWS (Blom JD, 2016)

STEP 1: Distinguish the symptom from other perceptual disorders such as hallucinations and illusions.

STEP 2: Identify the etiological factor, responsible for the symptoms.

STEP 3: Establish, whether the identified etiological factor is responsible for triggering the symptoms.

TREATMENT

Alice in Wonderland Syndrome has no proven effective treatment. In most of the cases therapy is considered useful and necessary to treat the suspected underlying medical conditions (Blom JD, 2016; Palacios-Sanchez L *et al*., 2018). Through many scientific reviews, it has been found that the most common cause is migraine, followed by infections and then epilepsy (Mastria G *et al*., 2016). Antibiotics and antiepileptic are the best choice to treat the infections and epileptic condition (Palacios-Sanchez L *et al*., 2018). Migraine can be treated by using an adequate prophylactic treatment with proper diet. When a study had been conducted on the treatment of migraine, it was concluded that the verapamil has shown 55% effectiveness where as valproic acid has shown only 15% (H B *et al*., 2018). For the migraine induced AIWS, valproic acid is shown to be more beneficial. Dose of valproic acid: 500mg/day administered initially, then increased to 1000mg/day (Evans RW, Lipton RB, 2001). Antipsychotics are rarely prescribed, especially in psychotic patients with distortions as comorbid symptoms, since they can be aggravated by the use of antipsychotics (Blom JD, 2016).

CONCLUSION

Alice in Wonderland Syndrome is still unknown and remains undiagnosed because of the lack of universally accepted diagnostic criteria. The treatment can be given only for the underlying suspected cause, if the physician is not familiar with the syndrome, the diagnosis may be missed and hence leads to more complications. This article emphasize the relevance of the rare neuropsychological condition and bring more awareness among the healthcare sector and in our society.

ACKNOWLEDGEMNET

Nil.

CONFLICT OF INTEREST

None.

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Cite this article:
Naiema Shajihan, Shijin VS, Tijo PS, Vismaya VR, Kavitha TR, Parvathy Nandan and Lallu Mariam Jacob. Alice In Wonderland Syndrome: A Review. *International Journal of Pharmacy & Therapeutics*, 10(3), 2019, 61-64.
DOI: **http://dx.doi.org/10.21276/ijpt.2019.10.3.1**